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Effects of Nicotine on Finger Tapping Rate in Non-Smokers

R. J. WEST[1]

Department of Psychology, Royal Holloway and Bedford New College, London University

AND

M. J. JARVIS

Addiction Research Unit, Institute of Psychiatry, Denmark Hill, London SE5

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WEST, R. J. AND M. J. JARVIS. *Effects of nicotine on finger tapping rate in non-smokers.* PHARMACOL BIOCHEM BEHAV **25**(4) 727–731, 1986.—Five experiments were conducted investigating the effects of nicotine on finger tapping rate in non-smokers. In each experiment subjects tapped as fast as possible a fixed number of times with one finger on a conventional computer keyboard. In the first experiment tapping rate was increased by two 2 mg doses of a nasal nicotine solution (NNS) but not by an inactive solution. The second study was carried out double-blind and showed that a single 2 mg dose of NNS improved tapping performance by about 5% whereas a very low dose (0.15 mg) NNS and a placebo had no effect. The effect of the NNS was to bring about a sustained increase in tapping rate from the start of each trial. The third study found that the effect of nicotine on tapping was reduced by a single 2.5 mg dose of the central cholinergic blocking agent, mecamylamine, but not by a placebo. Experiment four followed tapping rate for one hour after a dose of two 2 mg NNS and showed that within a subject this behavioural measure can provide a very consistent and sensitive bio-assay of the time course of nicotine effects. The final experiment found that repeated dosing with one 2 mg NNS on an hourly schedule for six hours produced a reliable increase in tapping speed after each dose with no evidence of acute tolerance. The results indicate that nicotine can substantially improve performance by non-smokers on a simple motor task, probably via its action on cholinergic pathways. NNS provides for the first time an effective means of examining the effects of nicotine on non-smokers.

Nicotine Finger tapping Non-smokers

PHYSIOLOGICALLY, nicotine appears to have primarily stimulant actions. It increases adrenaline and cortisol output and raises blood pressure and heart rate [1, 7, 16]. It appears to reduce alpha activity in the EEG and increase the dominant alpha frequency [3,6]. There is also evidence that it has stimulant actions on some perceptual tasks. It increases the critical flicker-fusion threshold [11] and may help to sustain concentration in long symbol recognition tasks [13]. As yet there is little evidence that nicotine has similar effects on simple motor tasks.

One problem with assessing the effects of nicotine on performance is that ideally one wants to use non-smokers who have not had a chance to build up a tolerance to its effects, yet it has been difficult to find a means of administering nicotine to non-smokers. Cigarettes are of little value because non-smokers find the smoke too irritant to inhale. Nicotine chewing gum induces nausea. Nicotine tablets have been used [2, 12, 13] but these are a poor means of delivery because swallowed nicotine is not well absorbed and most of what is ingested is metabolised in the first pass in the liver. Crushing the tablets and holding them in the mouth may allow some buccal absorption but levels are likely to be very low.

Recently a technique of dosing non-smokers with nicotine has been developed which can provide a moderate dose relatively quickly. This method involves placing a droplet of a nicotine solution in the nose by means of a special single-dose applicator [9]. This "nasal nicotine solution" (NNS) can give rise to plasma nicotine concentrations of between a third and one whole cigarette. Plasma nicotine concentrations peak 7 to 10 minutes after the dose. We have examined the effects of NNS on a simple motor task—tapping with one finger on a key as fast as possible. Our subjects were non-smokers because we wanted to determine the effects of nicotine without the complications of possible chronic tolerance effects.

Finger tapping is one of the simplest motor activities. It has been reported that tapping rate can be increased by stimulant drugs such as methylphenidate and impaired by a range of conventional depressant drugs including butobarbitone [4]. One study has looked at the effects of nicotine on tapping rate in non-smokers [2]. However, this study used

[1]Requests for reprints should be addressed to R. West, Department of Psychology, Royal Holloway and Bedford New College, Egham Hill, Surrey, UK TW20 OEX.

TABLE 1

TAPPING RATES IN 8 SUBJECTS BEFORE AND AFTER TAKING TWO 2 mg DOSES OF NASAL NICOTINE SOLUTION AND AN INACTIVE SOLUTION

	Nasal Nicotine		Inactive Solution	
	Baseline	Post-dose	Baseline	Post-dose
Mean	389.8	406.1*	390.9	393.5
SD	49.8	43.3	45.0	46.4
% Increase		4.2		0.7

*Significant increase from baseline ($p<0.01$, Binomial).

TABLE 2

TAPPING RATES IN 8 SUBJECTS BEFORE AND AFTER 2 mg NASAL NICOTINE (NNS), 0.15 mg NNS AND INACTIVE PLACEBO

	2 mg NNS		0.15 mg NNS		Placebo	
	Baseline	Post-dose	Baseline	Post-dose	Baseline	Post-dose
Mean	427.4	448.2*	434.1	432.6	424.8	428.1
SD	29.4	39.4	33.7	37.0	31.2	33.2
% Increase		4.9		−0.3		0.8

*Significant increase from baseline ($p<0.01$, Binomial), greater than increase after 0.15 mg NNS ($p<0.01$, Binomial) and placebo ($p<0.05$, Binomial).

nicotine tablets. Given the poor absorption from tablets and the fact that they only contained 0.1 mg of nicotine, they must have been no more than placebos. It is not surprising, therefore, that there was no increase in tapping rate. If nicotine's other stimulant actions are also reflected in motor performance, then the NNS should increase tapping rate.

EXPERIMENT 1

Experiment 1 was designed to determine whether NNS would increase maximum tapping rate by comparison with an inactive solution.

Subjects, Method and Results

The subjects were eight male non-smoking volunteers aged from 29 to 55 years. Each subject performed all conditions. In one condition the subjects performed a tapping task before and 10 minutes after taking two 2 mg doses of NNS. The tapping task required subjects to tap with the forefinger of their dominant hand as fast as possible 300 times on a single key of a Model B 'BBC' computer keyboard. The subjects were allowed to tap in any way they wished, using their whole arm if necessary. The computer automatically terminated the trial after 300 taps and recorded the tapping rate in taps per minute. There were no practice trials. In the second condition an inactive nasal solution containing a pepper extract was used instead of the nasal nicotine. The pepper extract was to mimic some of the local irritancy of the nicotine in the nose.

The order of the two conditions was balanced and each condition took place on a separate day. Non-parametric tests were used to compare conditions. In view of nicotine's other stimulant actions one-tailed tests were used, looking for an increase in tapping rate.

Tapping rate increased after the NNS in all subjects ($p<0.01$, Binomial) whereas after the inactive nasal solution there was no trend either way (Table 1). The increase after NNS averaged 4 percent of baseline performance.

EXPERIMENT 2

In order to confirm the findings of the previous study and to ensure that the result was not due to a placebo effect we conducted a second study in which a single 2 mg dose of NNS was compared with a very small nicotine dose (0.15 mg) and a pepper placebo. This study was carried out double-blind. We were also interested to know whether the very low dose of nicotine could enhance performance on the tapping task.

Subjects, Method and Results

The subjects were seven male and one female non-smoking volunteers aged from 26 to 55 years. All the subjects underwent three conditions. In each condition they first performed three practice trials of the tapping task with each trial requiring 200 taps. After a rest of a minute they performed three baseline trials. They then took either one 2 mg NNS or one 0.15 mg NNS or one inactive nasal solution containing pepper extract. After a wait of 5 minutes they performed a further three trials of the tapping task. The means of the three baseline and three post-NNS trials were taken as the pre-drug and post-drug scores respectively. All the conditions were undergone on the same day with at least two

TABLE 3

TAPPING RATES IN 5 SUBJECTS BEFORE AND AFTER NASAL NICOTINE (NNS) WHILE ON 2.5 mg MECAMYLAMINE AND PLACEBO

	A: Mecamylamine			
	Pre-mecamylamine		Post-mecamylamine	
	Pre-NNS	Post-NNS	Pre-NNS	Post-NNS
Mean	396.6	415.9	402.7	411.8*
SD	32.1	35.8	36.3	37.0
% Increase		4.9		2.3

	B: Placebo			
	Pre-placebo		Post-placebo	
	Pre-NNS	Post-NNS	Pre-NNS	Post-NNS
Mean	398.7	417.3	404.9	417.9†
SD	36.0	33.8	28.5	33.7
% Increase		4.7		3.2

*Increase after NNS significantly less post-mecamylamine than pre-mecamylamine ($p<0.05$, Binomial).

†No difference between increase after NNS pre- and post-placebo.

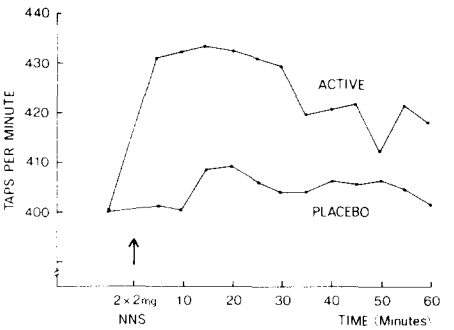

FIG. 1. Tapping rate over one hour in a single subject after receiving active (2×2 mg) and placebo NNS.

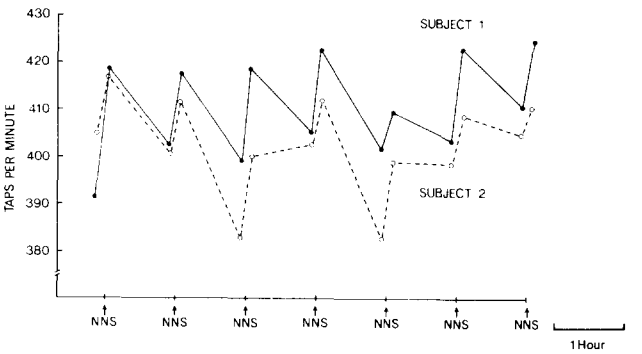

FIG. 2. Tapping rate in two subjects over six hours when NNS (2 mg) was given on an hourly schedule.

hours intervening between each one. The experiment was conducted double-blind.

All eight subjects showed an increase in tapping rate after the 2 mg NNS ($p<0.01$, Binomial) whereas there was no consistent trend with either the 0.15 mg NNS or the inactive solution. The increase after NNS averaged 20.8 taps per minute, or 5 percent over baseline, and was significantly greater than after either 0.15 mg NNS or placebo ($p<0.01$ and $p<0.05$ respectively, Binomial) (Table 2).

EXPERIMENT 3

There is evidence that nicotine acts on cholinergic receptor sites in the CNS and autonomic nervous system [8]. The cholinergic antagonist, mecamylamine, has been shown to reduce at least some of nicotine's effects [14]. We conducted a further experiment to determine whether a small dose of this drug would reduce the effect of nicotine on tapping rate.

Subjects, Method and Results

The subjects were four male and one female non-smoking volunteers aged between 26 and 55 years. There were two conditions with each subject undergoing both. In one condition the subjects performed six trials of the tapping task before and after taking one 2 mg nasal nicotine solution. Each trial required subjects to tap 200 times and was followed by a 30–60 sec rest. Then the subjects took a capsule containing 2.5 mg mecamylamine. After waiting two hours to give the mecamylamine time to work, the subjects took another 2 mg nasal nicotine solution performing six tapping trials before and after as previously. The second condition was identical except that a placebo was substituted for the mecamylamine. Neither the experimenter nor the subjects knew whether mecamylamine or placebo was being taken. The order of the conditions was randomized. The tapping rate in each six-trial block was averaged. It was expected that nasal nicotine would increase tapping rate and mecamylamine would reduce this effect.

In all five subjects the tapping rate was higher after taking the NNS than before it on every occasion that the nicotine was taken (Table 3). In all the subjects, this increase was smaller two hours after taking the mecamylamine than beforehand ($p<0.05$, Binomial). There was no consistent trend with the placebo. The tapping rate after taking the nasal nicotine was lower in every case when subjects were on mecamylamine than when they were on placebo ($p<0.05$, Binomial).

EXPERIMENT 4

This experiment followed the time course of the effect of NNS on tapping rate in a single subject. The aim was to assess the sensitivity and consistency of the tapping measure and the duration of the nicotine effect.

Subject, Method and Results

A single, non-smoking, male subject aged 45 took part in this study. A baseline measure of tapping rate was taken with the subject performing 300 taps. He then took two 2 mg NNS and performed the tapping task after 6, 9, 11, 16, 21, 26, 31, 36, 41, 46, 51, 56 and 61 minutes. On another day this procedure was repeated except that inactive nasal solution was substituted for NNS. The results are shown in Fig. 1. Tapping rate rose from 400 per minute before NNS to 437 per

minute 11 minutes after the dose. It remained consistently elevated up to 30 minutes and then began to decline, but was still above baseline levels after one hour. After the inactive solution there was no change in tapping rate.

EXPERIMENT 5

This experiment sought to determine whether the effect of NNS would be maintained with repeated dosing on an hourly schedule or whether after the first few doses acute tolerance would occur.

Subjects, Method and Results

Two male, non-smoking subjects took part in this experiment. They performed two trials of the tapping task (with 300 taps per trial) before and two trials after taking one 2 mg NNS every hour from 9.45 a.m. to 3.45 p.m. (seven doses in all). The post NNS trials were performed seven and 10 minutes after the doses. The pre-dose trials and post-dose trials were averaged for each dose. The results are shown in Fig. 2. It is evident that the NNS increased tapping rate after every dose in both subjects. The mean increase in tapping rate was 3.2% over baseline in one subject and 4.1% in the other. There was no sign of a lessening of the effect with later doses.

DISCUSSION

In all five experiments, the administration of 2 mg nasal nicotine solution (NNS) reliably enhanced finger tapping rate. The increase from a single 2 mg dose was about 5%. There was no increase from a placebo or a single 0.15 mg dose. The effect of NNS was reduced though not obliterated by a small dose (2.5 mg) of mecamylamine. The increase in tapping rate after NNS was shown to last for at least 30 minutes and there was no evidence of acute tolerance with repeated dosing on an hourly schedule.

The size of the effect of NNS on tapping rate was substantial and must have been due to nicotine. By no means is all of the nicotine in NNS absorbed. After a single 2 mg dose it is unlikely that more than 1 mg enters the blood on average [15]. Thus a nicotine dose considerably less than that from a single cigarette can substantially improve performance on a simple motor task in non-smokers. This does not mean that smokers would necessarily experience a similar increase. For example, it may be that this effect of nicotine is subject to tolerance. If so, it may be necessary for the smoker to continue smoking to prevent a deterioration in performance below normal levels; and/or only the first cigarette of the day may have an appreciable performance-enhancing effect.

Nicotine is known to increase hand tremor and it might be argued that our results are due to this. However, this cannot be the case because the keyboard used for the tapping task was sprung and required more force than would be available from an exaggerated tremor. Moreover, the speed of tremor is considerably faster than our subjects' maximum tapping rate [10].

Mecamylamine has been shown to reduce the effects of nicotine on a variety of physiological measures. The finding that mecamylamine reduced the effect of nicotine on tapping rate suggests that similar cholinergic pathways are involved in the actions of nicotine on tapping as on other variables. The dose of mecamylamine used in this study was small and it is possible that complete blockade would be achieved with a larger dose.

The results of Experiment 4 showed that the effects of NNS are not fleeting and occur for as long as there is nicotine in the blood. They also show that the measure is sensitive enough to chart the time course of nicotine's effects. The fact that we could find no attenuation of the nicotine-induced increase in tapping rate with repeated dosing suggests that the hourly schedule we used did not lead to acute tolerance to nicotine's effects, at least in the course of one day. This does not rule out the possibility that continuing such a regime for longer than one day would not lead to longer-term tolerance. Tolerance has been observed to some other effects of nicotine such as dizziness [5].

The fact that nicotine enhances performance on a simple motor task does not mean that it necessarily improves more complex information processing, although there have been reports that this may be the case [13]. It does indicate, however, that it may be worth looking at the effects of nicotine on physical abilities such as muscular strength, speed of muscle movement or endurance. If nicotine were found to have performance enhancing effects in these areas its use by sportsmen might confer an unfair advantage. A case could then be made for including it in the category of drugs proscribed in sport.

In conclusion, this series of experiments reveals that nasal nicotine can deliver nicotine in sufficient amounts to produce strong and consistent effects on a simple motor task. The way is now open to explore the effects of nicotine on a variety of performance measures involving perceptual, motor and cognitive processes to assess the role that it may play in maintaining smoking.

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REFERENCES

1. Cryer, P. E., M. W. Hammond, J. V. Santiago and S. D. Shah. Norepinephrine and epinephrine release and adrenergic mediation of smoking-related hemodynamic and metabolic events. *N Engl J Med* **295:** 573–577, 1976.
2. Frith, C. D. The effects of nicotine on tapping. *Life Sci* **6:** 321–326, 1967.
3. Herning, R. I., R. T. Jones and J. Bachman. EEG changes during tobacco withdrawal. *Psychophysiology* **20:** 507–512, 1983.
4. Hindmarch, I. Psychomotor function and psychoactive drugs. *Br J Clin Pharmacol* **10:** 189–209, 1980.
5. Jarvik, M. E. Tolerance to the effects of tobacco. In: *Cigarette Smoking as a Dependence Process. NIDA Research Monograph 23*, edited by N. A. Krasnegor. Washington: Department of Health, Education and Welfare, 1979.
6. Knott, V. J. and P. H. Venables. EEG alpha correlates of non-smokers, smokers smoking and smoking deprivation. *Psychopharmacology (Berlin)* **14:** 150–155, 1977.
7. Myrsten, A.-L., B. Post, M. Frankenhaeuser and G. Johansson. Changes in behavioral and physiological activation induced by cigarette smoking in habitual smokers. *Psychopharmacologia* **27:** 305–312, 1972.

8. Romano, C. and A. Goldstein. Stereo-specific nicotine receptors on rat brain membranes. *Science* **210:** 647–649, 1980.
9. Russell, M. A. H., M. J. Jarvis, C. Feyerabend and O. Ferno. Nasal nicotine solution: a potential aid to giving up smoking? *Br Med J* **286:** 683–684, 1983.
10. Shiffman, S. M., E. R. Gritz, J. Maltese, M. A. Lee, N. G. Schneider and M. E. Jarvik. Effects of cigarette smoking and oral nicotine on hand tremor. *Clin Pharmacol Ther* **33:** 800–805, 1983.
11. Waller, D. and S. Levander. Smoking and vigilance: the effects of tobacco on CFF as related to personality and smoking habits. *Psychopharmacology (Berlin)* **70:** 131–136, 1980.
12. Warwick, K. M. and H. J. Eysenck. Experimental studies of the behavioural effects of nicotine. *Pharmakopsychi Neuropsychopharmakol* **1:** 145–169, 1968.
13. Wesnes, K. and D. M. Warburton. Smoking, nicotine and human performance. *Pharmacol Ther* **21:** 189–208, 1983.
14. West, R. J. and M. A. H. Russell. Nicotine pharmacology and smoking dependence. In: *Psychopharmacology: Recent Advances and Future Prospects,* edited by S. Iversen. Oxford: Oxford University Press, 1985.
15. West, R. J., M. J. Jarvis, M. A. H. Russell and C. Feyerabend. Plasma nicotine concentrations from repeated doses of nasal nicotine solution. *Bri J Addict* **79:** 443–445, 1984.
16. Wilkins, J. N., H. E. Carlson, H. Van Vunakis, M. A. Nill, E. Gritz and M. E. Jarvik. Nicotine from cigarette smoking increases circulating levels of cortisol, growth hormone and prolactin in male chronic smokers. *Psychopharmacology (Berlin)* **78:** 305–308, 1982.